

XX MO9826061-A2.
XX
XX 18-JUN-1998.
XX
XX 08-DEC-1997; 97WO-US22740.
XX PF
XX 01-DEC-1997; 97US-0982272.
XX PR
XX 09-DEC-1996; 96US-0032145.
XX
XX (REGC) UNIV CALIFORNIA.
XX
XX Cantwell M, Kipps TJ, Sharma S;
PI
XX MPI; 1998-348521/30.
DR
XX
PT Vectors containing accessory molecule ligand genes - used for
altering immunoreactivity of cells, particularly for treatment of
neoplasia or autoimmune disorders, e.g. rheumatoid arthritis

Disclosure: Page 118; 167pp; English.

The present sequence represents a nerve growth factor gene. The sequence is used to exemplify the method of the invention. The specification describes a method for altering the immunoreactivity of human cells which comprises introducing a gene encoding an accessory molecule ligand (AML) into the cells so that the AML is expressed on the surface of the cells. Vectors containing the AML genes can be used in gene therapy for treating neoplasia or autoimmune disorders such as rheumatoid arthritis. They can also be used for vaccination to produce immunity against a virus cell, bacteria, protein, fungus or neoplasia.

Sequence 1176 BP; 283 A; 330 C; 295 G; 268 T; 0 other;

| | | | | |
|-----------------------|--------------|--------------------|-----------------|--------------|
| Query Match | 25.0%; | Score 99.6; | DB 19; | Length 1176; |
| Best Local Similarity | 58.4%; | Pred. No. 6,3e-22; | | |
| Matches 223; | Conservative | 0; | Mismatches 114; | Indels 45; |
| | | | Gaps | 1 |

| | | | |
|----|-----|--|------|
| OY | 5 | ccaacgactcttgcacgcgycggaagtactctgtgtgtacagcgaagagcactggttg | 64 |
| | | | |
| Db | 664 | ccacacccactctccacatgtaggtctcgaagtgtgtacagtgccagtggtgttg | 723 |
| OY | 65 | gcaactcgaccacaagccacagacttaccgvggcaagaagtccagtggtccacatgttc | 124 |
| | | | |
| Db | 724 | gagaaagaacccacacacacaaagacacaaaggacaaagagtgacagtgccgycgcgaagtba | 783 |
| OY | 125 | gcatcaacaacagctggtgaaagaagcagatgtctacagagaccacgtgtccgtgtgcgaagc | 184 |
| | | | |
| Db | 784 | acattacaacaacagtgattacagacagtaacttttttgagacacagtgccgagctccaacc | 843 |
| OY | 185 | ccatcgvgggcccccacagccgvggtcaaggaagtacgcgcttaagcaggaacctagct | 244 |
| | | | |
| Db | 844 | ctgtgtgaagag-----tgggt | 858 |
| OY | 245 | gtcgtgggatacgacaacgagcactgtgaactcttatatgcacaacgtgcacaccttgtgc | 304 |
| | | | |
| Db | 859 | gccgvggcatgcagctccacaacacttggaaactatactatgcaccagactcacaccttcgtca | 918 |
| OY | 305 | gggcgttaacgctcctacaanaaacagatgtccctggaggtttcatccgaatcaaacgcgcctt | 364 |
| | | | |
| Db | 919 | agcgcttgacaacagatgtaggaagcagctgcgtcgtgggttcacgcgatatgacaacagcct | 978 |
| OY | 365 | ggcgtgtgcctcagccgcaa | 386 |
| | | | |
| Db | 979 | gtcgtgtgtgtctcagcagaa | 1000 |

| RESULT | 4 |
|--------|-------------------------------|
| N40031 | |
| ID | N40031 standard; DNA; 1164 BP |
| XX | |
| AC | N40031; |

| | | | |
|-----|---|---------------------|--|
| XX | 25-JAN-1992 | (first entry) | |
| DT | | | |
| XX | | | |
| DE | Sequence of the human beta-nerve growth factor (NGF) gene and | | |
| DE | flanking regions on phage lambda h-beta-N8. | | |
| KW | Nerve damage; therapy; ss. | | |
| XX | | | |
| OS | Homo sapiens. | | |
| XX | | | |
| FH | Key | Location/Qualifiers | |
| FT | sig_peptide | 75..635 | |
| FT | | /*tag= a | |
| FT | mat_peptide | 636..998 | |
| FT | | /*tag= b | |
| XX | | | |
| PM | EP121338-A. | | |
| XX | | | |
| PD | 10-OCT-1984. | | |
| XX | | | |
| PF | 02-MAR-1984; | 84EP-0301377. | |
| XX | | | |
| PPR | 03-MAR-1983; | 83US-0471962. | |
| XX | | | |
| PA | (GETH) GENENTECH INC. | | |
| XX | | | |
| PI | Gray AM, Ullrich A; | | |
| XX | | | |
| DR | WPI. 1984-2519C9/41. | | |
| DR | P-PSDB; P40036. | | |

Human beta-nerve growth factor free from other proteins - obt'd. by recombinant DNA techniques for treating nerve damage

Example; Fig 2; 42pp; English.

The inventors claim human beta-nerve growth factor (NGF) free from other proteins of human origin. Also claimed are the DNA sequence encoding human beta-NGF operably linked with a DNA sequence capable of effecting its expression in a recombinant host cell; a replicable expression vector contg. the DNA; and host cells transformed with the vector. The plasmid claimed is plasmid p-beta-NGF trip 1. Using the plasmid, larger amounts of pure beta-NGF are obtainable than by extrn. of natural materials, see e.g. Ep--2139.

Sequence 1164 Bp; 284 A; 327 C; 284 G; 269 T; 0 other;

```

Query Match 24.6%; Score 98; DB 5; Length 1164;
Best Local Similarity 58.1%; Pred. No. 2e-21;
Matches 222; Conservative 0; Mismatches 115; Indels 45; Gaps 1

QY 5 ccaacgactcttgatcgcgcgagtaactctgtgtgtacagcgaagagcactggttg 64
   ||| ||||| || ||||| ||||| ||||| ||||| |||||
Db 643 cccaccacgactctccacataggggggttctcaigtgtgtacaggtgtcagtgttg 702
   ||| ||||| || ||||| ||||| ||||| ||||| |||||

QY 65 gcaacctgacccaagccacagacttaacgggcaatgaatcagctgtcgtccacatgttc 124
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 703 gggatagaagccacagccacacagactcaagaaggcaagaggtgacagtgtcgtccgagtgta 762
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

QY 125 gcatcaacaacagtgtgtgaagaagcagatgttcttaagagacccagtgccgtgtgtcgaagc 184
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 763 acattacaacaacagttattacagacagttaattttttgaagccaaagtgcgagcctccaactc 822
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

QY 185 ccattgggggcccccaagccgggtcaagggttcaagcggttaagaaggaactcctcagtt 244
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 823 cgtgttgagag-----tggtt 837
   ||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

QY 245 gtctgtggagatcacacagacgtgaaactcttattatgcaccaacgtgcacaccttgtgc 304
   ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 838 gccgggggactgcacaccacacacgtgaaactatctatctgcacccacagactcaacaccttcgtca 897
   ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

QY 305 gggcggttaacgtctctacaaaaaacagatgtyccttgaggtttcatccgaatcaaacgccgctt 364
   ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

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Db      898 aggcgttcacacagatgagaagcaggctcgcttggtaggtccatccgatagcacagcct 957
          ||||| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Oy      365 gccgttgccctccacagcgcaa 386
          | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      958 gtgtgtgtgtgtctcagcagaa 979

RESULT   5
N40034    N40034 standard; DNA; 1164 BP.
AC        N40034;
XX        N40034;
DT        25-JAN-1992 (first entry)
DE        Sequence of human prepro-beta-nerve growth factor (NGF) gene.
KW        Nerve damage; therapy; ss.
XX        Homo sapiens.
FH        Key Location/Qualifiers
FT        sig_peptide       75..635
FT                               /*tag= a
FT                               636..998
FT        mat_peptide       /*tag= b
FT
PN        EP121338-A.
PD        10-OCT-1984.
XX
XX        PE        02-MAR-1984;      84EP-0301377.
XX
XX        PR        03-MAR-1983;      83US-0471962.
XX
PPA        (GETH ) GENENTECH INC.
PI        Gray AM, Ullrich A;
DR        WPI; 1984-251909/41.
DR        P-PDSB; P40039.
XX
PT        Human beta-nerve growth factor free from other proteins - obtd.
PT        by recombinant DNA techniques for treating nerve damage
PS
XX        Example; Fig 6; 42pp; English.
XX
CC        The inventors claim human beta-nerve growth factor (NGF) free from
CC        other proteins of human origin. Also claimed are the DNA sequence
CC        encoding human beta-NGF operably linked with a DNA sequence capable
CC        of effecting its expression in a recombinant host cell; a replicable
CC        expression vector contg. the DNA; and host cells transformed with
CC        the vector. The plasmid claimed is plasmid ph-beta-NGF trp 1. Using
CC        the plasmid, larger amounts of pure beta-NGF are obtainable than by
CC        extrn. of natural materials, see e.g. EP--2139.
CC
SQ        Sequence 1164 BP; 284 A; 327 C; 284 G; 269 T; 0 other;

Query Match      24.6%; Score 98; DB 5; Length 1164;
Best Local Similarity 58.1%; Pred. No. 2e-21;
Matches 222; Conservative 0; Mismatches 115; Indels 45; Gaps

Oy      5 ccaacgactcttcgcgcgcgaagtactctgtgtgtgtacagcgaaagacaactggttg 64
          || | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      643 ccacaccagctcttcacacatggggagttctcagttgtgacagttcagttgtgtgttg 702
          || | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Oy      65 gaacctggccccaacgacacagacttacgggggaatgaattcacagtcggtgcacatgttc 124
          | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      703 ggagataagaccacagccacacagacatcaagggaagtgagtaagtgctgcgcgaagtga 762
          | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Oy      125 gcatcaacaacgtgtgtgaagaagacagatgtttctaagagacacacgtgcgtgttcgaagc 184

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| | | | |
|-----------------------|--|--|-----|
| Dd | 763 | acatataacaagtgatattcagacaagctactttttagaccacaagcgagccctcaatc | 822 |
| Oy | 185 | ccatcggggcgccccaagccgggtcaaggatcagcgcgcttaagaagaaaccttaagt | 244 |
| Dd | 823 | ctgttgagag-----tggt | 837 |
| Oy | 245 | gtcgtggagtcgacaacgagcacctgaaccttatcttgaccacaagcttgacaccttgc | 304 |
| Dd | 838 | gcccggggatcgcactccacaaccttgaaactatatctgacacagcatcacaccttcga | 897 |
| Oy | 305 | gggcgtlaacgtlctacaaaacacagattgccttgagggtlcatccgaatcaagccgclt | 364 |
| Dd | 898 | agcgcttgacaacagatgagaagcagcgcttgcttgagggtatccggtatgacacagcct | 957 |
| Oy | 365 | gcgtgtgcgtcctcagccgcaa | 386 |
| Dd | 958 | gttgtgtgtgtctcagcaggaa | 979 |
| RESULT | 6 | | |
| ID | Q54282 | standard; CDNA; 1164 BP. | |
| XX | Q54282; | | |
| DT | 20-JUN-1994 | (first entry) | |
| DE | Cloned mouse pre-pro nerve growth factor cDNA. | | |
| KX | Mature human; beta-nerve growth factor; mouse; pre-pro portion; | | |
| KW | expression; NGF; hNGF; treatment; Alzheimer's Disease; murine; ss. | | |
| XX | Mus musculus. | | |
| OS | | | |
| FH | Key | Location/Qualifiers | |
| FT | CDS | /75..998 | |
| FT | | /*tag= A | |
| XX | US5272063-A. | | |
| PN | | | |
| XX | 21-DEC-1993. | | |
| XX | 20-JUN-1989; | 89US-0383118. | |
| PE | | | |
| XX | 22-NOV-1988; | 88US-0274878. | |
| PR | 20-JUL-1989; | 89US-0383118. | |
| XX | (SYNT) SYNTAX USA INC. | | |
| PA | Baecker PA, Barnett JW, Bursztyl-Petegrew H, Chan HW, Nguyen BT, | | |
| PI | P Ward C; | | |
| DR | MP1:1993-413401/51. | | |
| DR | P-PSDB; R45240. | | |
| XX | | | |
| XX | Prod'n. of active mature human beta-nerve growth factor in insect | | |
| PT | cells - using baculovirus expression system, and potential use of | | |
| PT | recombinant hNGF in treatment of Alzheimer's disease | | |
| XX | | | |
| PS | Disclosure; Fig 1; 23pp; English. | | |
| CC | The sequence is that of mouse pre-pro nerve growth factor cDNA | | |
| CC | which was used in a method of producing biologically active mature | | |
| CC | human beta-nerve growth factor in insect cells. | | |
| XX | | | |
| SO | Sequence 1164 BP; 285 A; 326 C; 283 G; 270 T; 0 other: | | |
| Query Match | 24.6%; Score 98; DB 14; Length 1164; | | |
| Best Local Similarity | 58.1%; Pred. No. 2e-21; | | |
| Matches | 222; Conservative 0; Mismatches 115; Indels 45; Gaps 1; | | |

PD 15-NOV-1994.
 XX
 PF 14-FEB-1991; 91JP-0021181.
 XX
 PR 31-AUG-1990; 90JP-0231317.
 XX
 PA (TAKE) TAKEDA CHEM IND LTD.
 XX
 DR WPI; 1995-033116/05.
 DR P-PSDB; R66688.
 XX
 PT Polyclonal antibody against human nerve growth factor (NGF) -
 XX useful to detect human NGF, for diagnosis of disease
 PS
 PS Example 1; Pages 31-33; 35pp; Japanese.
 CC 079871 encodes R66688 human nerve growth factor (hNGF), the
 CC protein was used as an immunogen to generate a polyclonal
 CC antibody against hNGF. The polyclonal antibody can be used
 CC to detect and determine hNGF pref. by enzyme immunoassay.
 SC
 Sequence 972 BP; 211 A; 293 C; 249 G; 219 T; 0 other;
 Query Match 22.8%; Score 91; DB 16; Length 972;
 Best Local Similarity 56.5%; Pred. No. 3e-19;
 Matches 221; Conservative 0; Mismatches 125; Indels 45; Gaps 1;

QY 5 ccaacgaactcttgatcgccgagcagatctctgtgtgacagcgaagacactggttg 64
 DB 568 cccatcccatctctccacagggcgagatctctcggtgtgtgacagcgtgtgtgtg 627
 QY 65 gaacactgaccccaagcagacagacttaccggtgacatgaagtcagctgtccacatgttc 124
 DB 628 gggataaagccacccgcacacagacatcaaggcgaagagtggtgtgtgtgtgtga 687
 QY 125 gcatcaacacagctgtgtgaagcagatgttctacagacacacgtgtgtgtgtgtga 184
 DB 688 acattacacacagtgatctacacacagtgatcttctgtgtgtgtgtgtgtgtgtgt 747
 QY 185 ccacgtggggcccccacagcgggtcgaagagtgacggtgttaagcaggaaccttagct 244
 DB 748 ccgtgtgacagcg-----ggt 762
 QY 245 gtccgtgtgacacgaacgacagcactgtgaactcttatgtcacacacgtgtcacaccttgtgc 304
 DB 763 gccgggggcatgtgacacagcactgtgaactcttatgtcacacacacacaccttgtgca 822
 QY 305 gggcgcttaacgtctcctcaaaaacacagattgctgtgtgtgtgtgtgtgtgtgtgtgt 364
 DB 823 aggcgctgtgacacatgt 882
 QY 365 ggcgt 395
 DB 883 gt 913

RESULT 9
 ID T05437 standard; DNA; 725 BP.
 AC T05437;
 XX
 XX 10-FEB-1996 (first entry)
 DE Human nerve growth factor gene.
 XX
 XX Nerve growth factor; neurotrophic factor; therapeutic;
 KW protein refolding; NGF; ss.
 XX
 XX Homo sapiens.
 XX
 FH Key Location/Qualifiers

FT misc-feature 1..342
 FT /tag= a
 FT /note= "NGF amino acids -121 to -20"
 FT misc-feature 345..723
 FT /tag= b
 FT /note= "NGF amino acids -19 to +120"
 XX
 XX W09530686-A1.
 XX
 XX 16-NOV-1995.
 PD
 XX
 PF 02-MAY-1995; 95WO-US05423.
 XX
 XX 27-JUN-1994; 94US-0266080.
 PR 09-MAY-1994; 94US-0240122.
 XX
 XX (SYNT) SYNTX-SYNERGEN NEUROSCIENCE JOINT VENTU.
 PA
 PI Bonam D, Kohno T, Lile J, Rosendahl MS;
 XX
 XX WPI; 1995-404080/51.
 DR P-PSDB; R77419..
 DR
 XX
 XX Process for bacterial expression of recombinant neurotrophic factor
 PT -useful for promoting the survival and maintaining phenotypic
 PT differentiation of nerve and glial cells.
 PS
 PS Claim 6; Page 32; 57pp; English.

XX The nerve growth factor (NGF) gene is expressed in Escherichia
 CC coli cells. The recombinant protein is solubilized and
 CC sulfonlated and allowed to refold in the presence of PEG and urea.
 CC Biologically active NGF, used for promoting the survival of and
 CC maintaining the phenotypic differentiation of nerve and glial cells,
 CC is isolated and purified. This method breaks incorrectly formed
 CC disulfide bonds and allows refolding of the factor into the correct
 CC tertiary structure required for maximum yield of full active protein.
 XX
 SQ Sequence 725 BP; 168 A; 207 C; 200 G; 150 T; 0 other;

Query Match 22.4%; Score 89.4; DB 16; Length 725;
 Best Local Similarity 56.3%; Pred. No. 8.6e-19;
 Matches 220; Conservative 0; Mismatches 126; Indels 45; Gaps 1;

QY 5 ccaacgaactcttgatcgccgagcagatctctgtgtgtgtgtgtgtgtgtgtgtgtgtgtgt 64
 DB 370 cccatcccatctctccacagggcgagatctctcggtgtgtgtgtgtgtgtgtgtgtgtgt 429
 QY 65 gaacactgaccccaagcagacacacttaccggtgacatgaagtcacagctgtgtgtgtgtgttc 124
 DB 430 gggataaagcaccgcacacagacatcaaggcgaagagtgatgtgtgtgtgtgtgtgtgtgt 489
 QY 125 gcatcaacacagctgtgtgaagcagatgttctacagacacacgtgtgtgtgtgtgtgtgtgt 184
 DB 490 acattacacacagtgatctacacacagtgatcttctgtgtgtgtgtgtgtgtgtgtgtgt 549
 QY 185 ccacgtggggcccccacagcgggtcgaagagtgacggtgttaagcaggaaccttagct 244
 DB 550 ccgtgtgacagcg-----ggt 564
 QY 245 gtccgtgtgacacgaacgacagcactgtgaactcttatgtcacacacgtgtcacaccttgtgc 304
 DB 565 gccgggggcatgtgacacagcactgtgaactcttatgtcacacacacacaccttgtgca 624
 QY 305 gggcgcttaacgtctcctcaaaaacacagattgctgtgtgtgtgtgtgtgtgtgtgtgtgt 364
 DB 625 aggcgctgtgacacatgt 684
 QY 365 ggcgt 395
 DB 685 gt 715

CC Human Ngr is useful as a reagent for study of the nervous system, and
CC for treatment of senile dementia. The DNA was derived from the human
CC gene or is synthesised chemically.
CC See also Q12639.
XX
XQ Sequence 972 BP; 212 A; 294 C; 248 G; 218 T; 0 other;

| | | | | |
|---------------------------|-------|-------------------|-------|-------------------|
| Query Match | 32.4% | Score 89.4 | DB 12 | Length 972 |
| Best Local Similarity | 56.3% | Pred. No. 9.6e-19 | | |
| Matches 220; Conservative | 0 | Mismatches 126 | | Indels 45; Gaps 1 |

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QY      5  ccacgactcttgcacgcgcgcgactctgtgtgtgcacgcgaagacactggcttg 64
      || | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db     568  ccacatcccatcttcacacagggcgcaattctcgtgtgtgcacagtctcagcgtgtggcttg 62

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D6
Q7 65 gcaacctgacccaaagccaacagacttacggggcgaatgatgcacgtctgcccacatgttc 120
| | ||||| ||||||| | ||||| | | ||||| | | ||||
D6 628 ggqgataagaccacccgccacagacatcaaggcgcaaggagtgtatgttctggagaagtgta 68

QY 125 gcatcaacaacgtggtgaagaagcagatgcttctaaggaccacagtgcggtgltcgaaac 18
||| || | ||| ||| ||| ||| ||| ||
Ph 688 acatttaaccaabtggtlataccaacaagttacttttttcagaccaagtgccggaccocaatc 74

185 ccacgcgggcgcccaagccggtcacaagagtcagcggcgcttaagcaggaacctagct 24
 ||| |
 248 cctttacacacg-----ggt 76

[illegible][illegible][illegible][illegible]

| | |
|--------|-------------------------------|
| Q10620 | |
| ID | Q10620 standard; DNA; 972 BP. |
| XX | |
| AC | Q10620; |

| | |
|----|---------------------------------|
| XX | 26-APR-1991 (first entry) |
| DT | |
| XX | |
| DE | Human nerve growth factor gene. |

| | |
|----|---------------------------|
| XX | NGF; senile dementia; ss. |
| KW | |
| XX | |
| OS | Homo sapiens. |

| | Key | Location/Qualifiers |
|----|----------------|---------------------|
| XX | | |
| FH | signal_peptide | 198..251 |
| FT | | |
| FM | | |

| | 252..923 |
|-------------|-----------------|
| CDS | /tag= b |
| FT | /label= pro-NGF |
| FT | 561..923 |
| FT | |
| mat peptide | |

| | | | |
|----|-------------|--------|---|
| FI | 1104-00000 | /*tag= | C |
| FT | | | |
| XX | | | |
| PN | EP414151-A. | | |
| xx | | | |

| | |
|----|-----------------------------|
| AA | 27-FEB-1991. |
| PD | |
| XX | |
| PF | 17-AUG-1990; '90EP-0115815. |

XX 21-AUG-1989; 89JP-0212980.
PR 20-DEC-1989; 89JP-0328198.
PR 13-APR-1990; 90JP-0096252.

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Page 11

